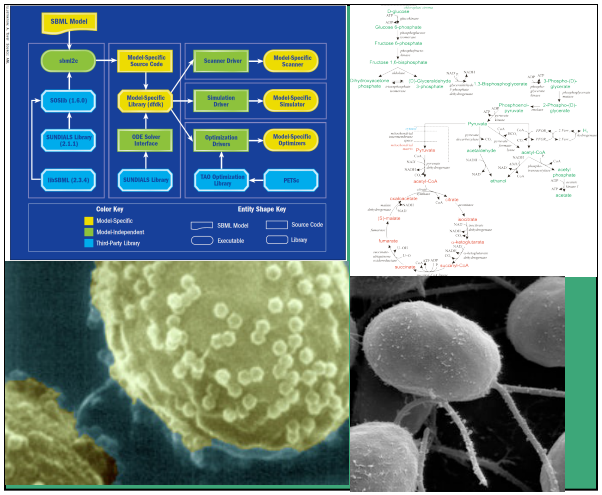
Pathways/Metabolic and Regulatory

Christopher H. Chang
Sr. Scientist,
Computational Science
NREL



Current Area of Research Interest

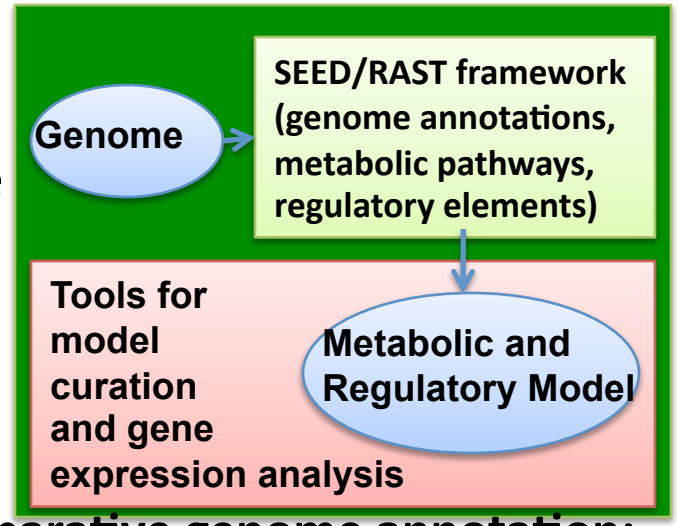
- Systems Biochemistry

Challenges that May be Addressed with Advanced Computing and Mathematics Capabilities

- Exploration, analysis, and visualization of abstract multidimensional spaces
- Metabolic graphs—algorithms and analyses
- Stochastic methods—agent-based modeling combined with kinetics
- Semantic technologies (Knowledgebase, AI) for model provenance and content

Pathways/Metabolic and Regulatory

Matt DeJongh
Associate Professor, Computer Science
Hope College, Holland, Michigan



Current Area of Research Interest

-> In the context of the SEED environment for comparative genome annotation:

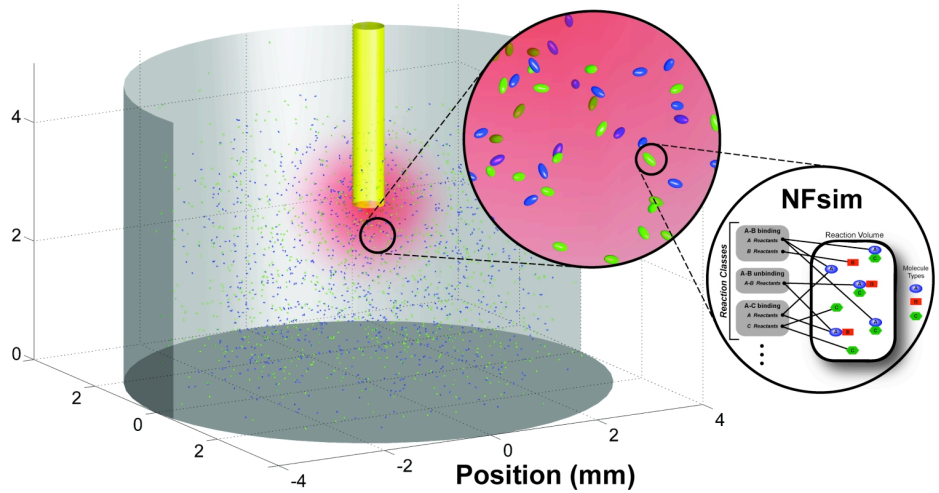
- Tools for creation and refinement of genome-scale metabolic models for prokaryotes
- Tools for identification of regulatory elements and integration with metabolic models
- Use of integrated models for gene expression data analysis

Challenges that May be Addressed with Advanced Computing and Mathematics Capabilities

- prediction of phenotype from genotype: biomass composition, transport capabilities, relationship of energy production pathways to environmental signals
- prediction of new metabolic and regulatory mechanisms
- exploration of the space of possible metabolisms

Pathways/Metabolic and Regulatory

Thierry Emonet
Assistant Professor
Yale University



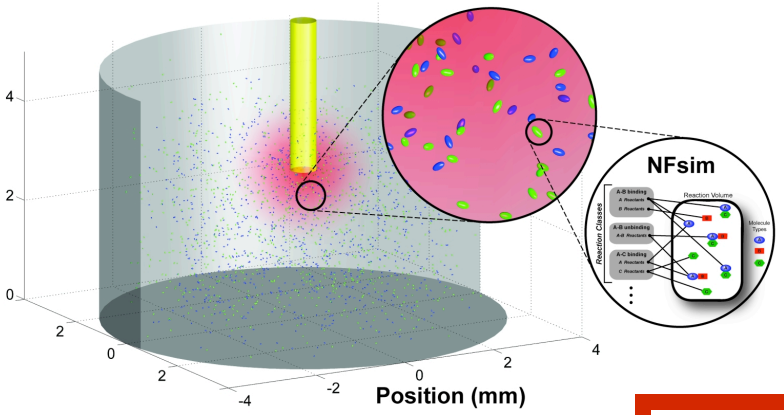
Current Area of Research Interest

- Digital assays and multiscale agent-based modeling to connect molecular mechanisms to cell behavior
- Dynamical encoding of odors by the fly
- The role of phenotypic variability in bacterial sensing
- The dynamical role of spatial localization in signal processing

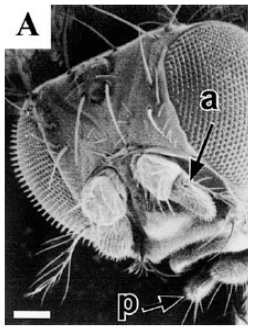
Challenges for Advanced Computing and Mathematics

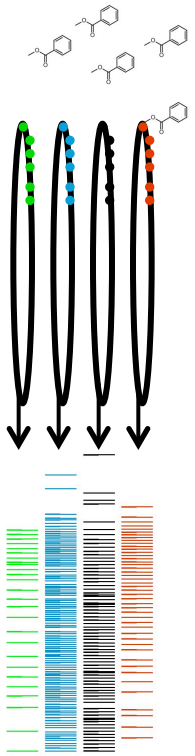
- Predicting cellular behavior from individuals to populations
- Accelerated stochastic agent-based simulation algorithms
- Automated dynamical model construction and parameter sensitivity analysis.

The role of individuality in clonal populations



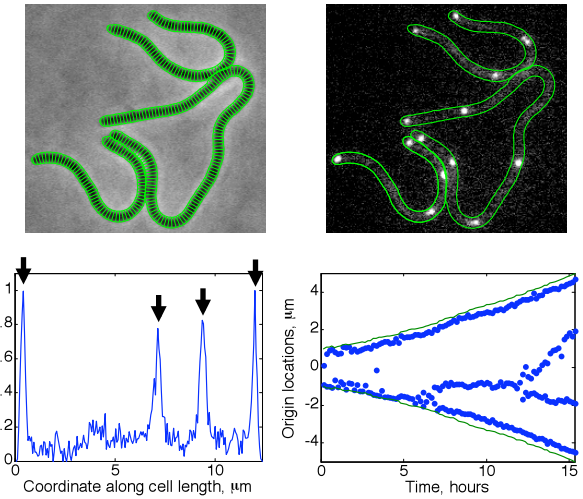
Temporal aspect of the odor code in *Drosophila*



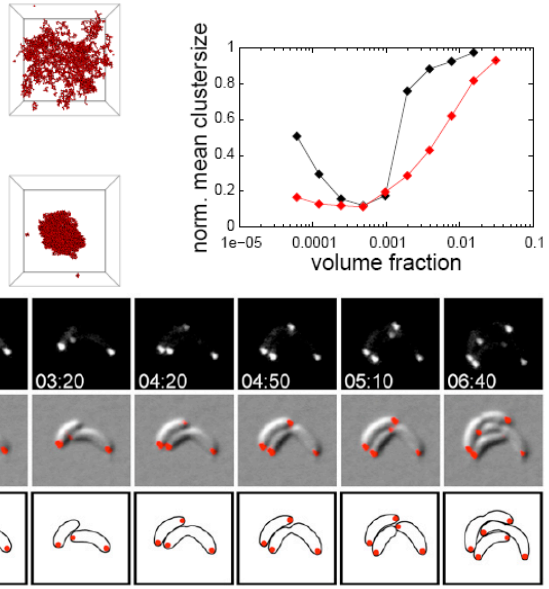


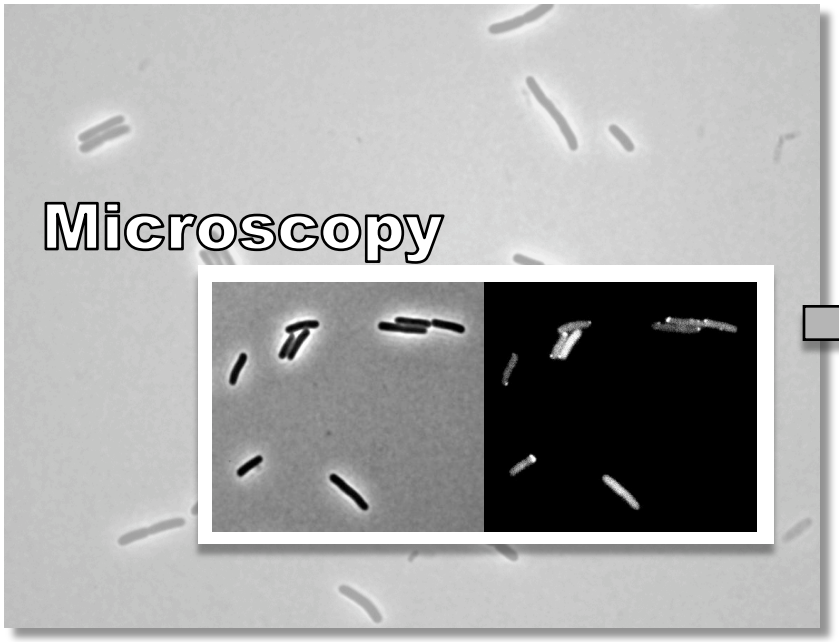
We study how live cells process information and make decisions using experiments, theory and modeling.

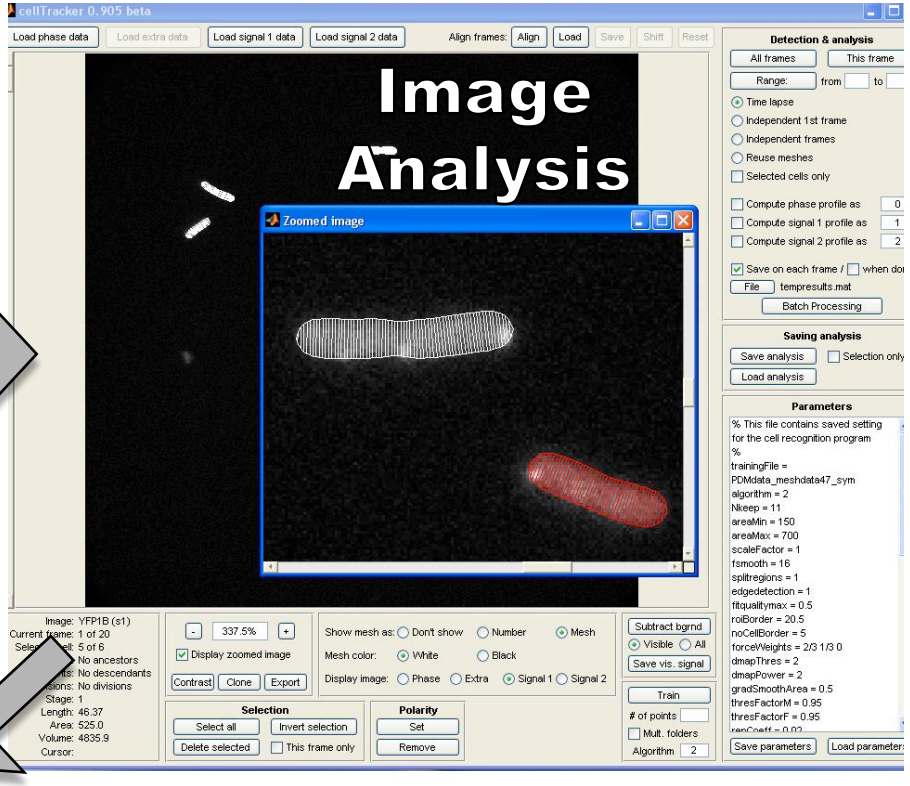
Stochastic dynamics of chromosome replication

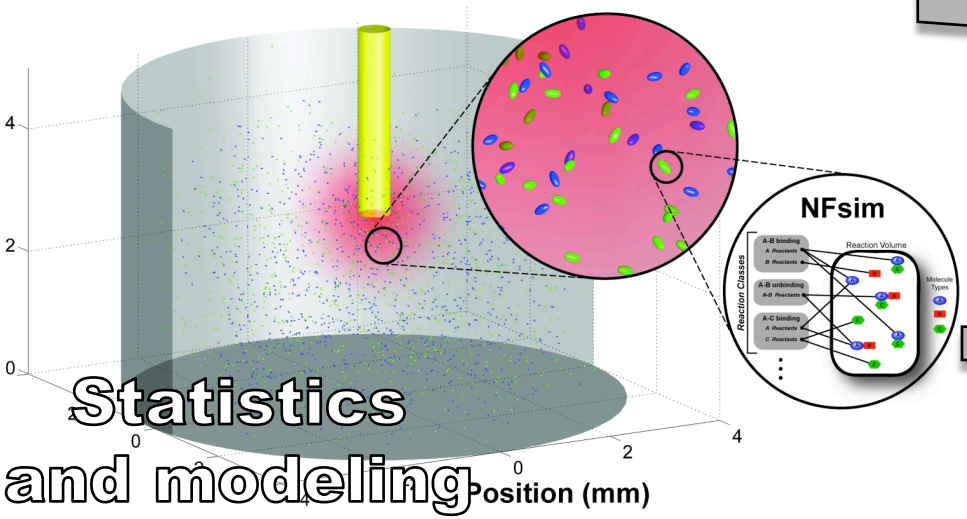


Self-aggregation mechanism for polar localization in bacteria

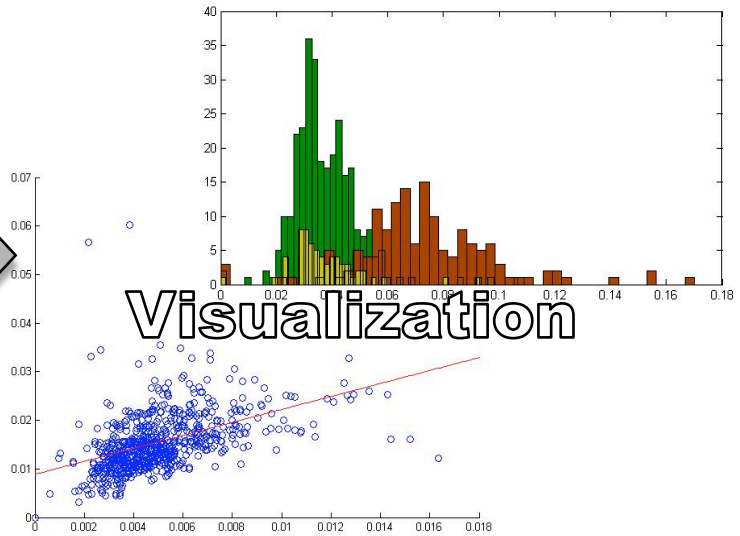








Statistics and modeling



Visualization

lab members

Roger Alexander
Postdoc
KBT 1054
(203) 432-3518
roger.alexander@yale.edu

Nicholas Frankel
Graduate Student in Rotation
KBT 1050
(203) 432-3517
nicholas.frankel@yale.edu

William Pontius
Graduate Student
KBT 1050
(203) 432-3517
william.pontius@yale.edu

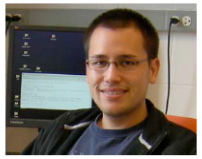
Adam Bildersee
Undergraduate Student
KBT 1050
(203) 432-3517
adam.bildersee@yale.edu

Garrit Jentsch
Postdoc
KBT 1054
(203) 432-3518
garrit.jentsch@yale.edu

Oleksii Sliusarenko
Postdoc
KBT 1050
(203) 432-3517
oleksii.sliusarenko@yale.edu

Thierry Emonet
Principal Investigator
KBT 1048
(203) 432-3516
thierry.emonet@yale.edu

Carlotta Martelli
Graduate Student
KBT 1054
(203) 432-3518
carlotta.martelli@yale.edu



Michael Sneddon
Graduate Student
KBT 1050
(203) 432-3517
michael.sneddon@yale.edu

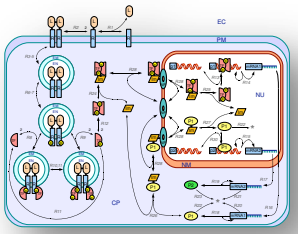
Collaborators

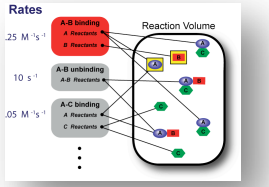
John Carlson, Yale
Philippe Cluzel and Heungwon Park, Harvard
James Faeder, University of Pittsburgh
Christine Jacobs-Wagner, Yale
Rick Stevens, Argonne National Laboratory

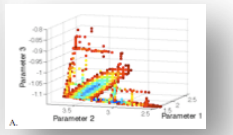
Funding

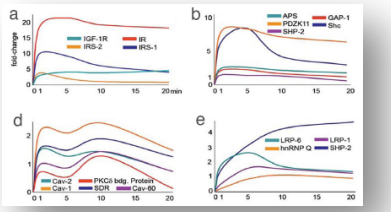
Alfred P. Sloan Foundation
NSF
National Academies Keck Futures Initiative

Large-Scale Simulation of Cell Signaling Networks with Robust Parameter Estimation and Experimental Design









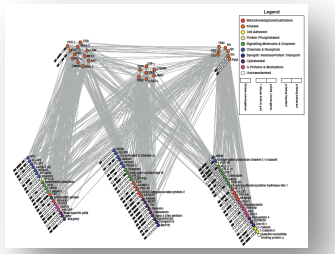
Large-scale Networks

Rule-based Models

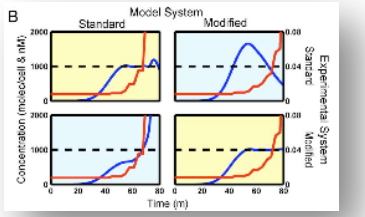
Rule-based Simulation

parameter estimation

Exptl. Data



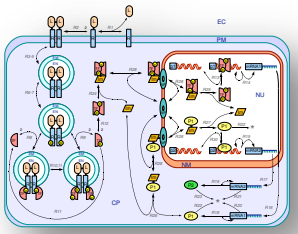
experimental design

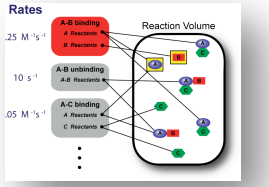


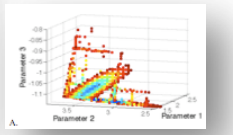
James Faeder
University of Pittsburgh
Department of Computational Biology

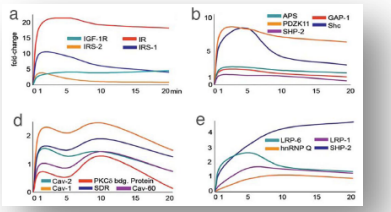
Collaborators
Thierry Emonet
William Hlavacek
Rick Stevens
Chris Langmead

Large-Scale Simulation of Cell Signaling Networks with Robust Parameter Estimation and Experimental Design









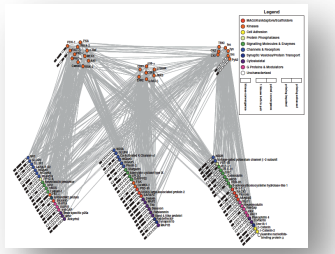
Large-scale Networks

Rule-based Models

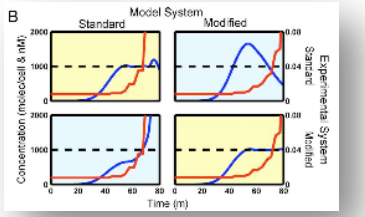
Rule-based Simulation

parameter estimation

Exptl. Data



experimental design

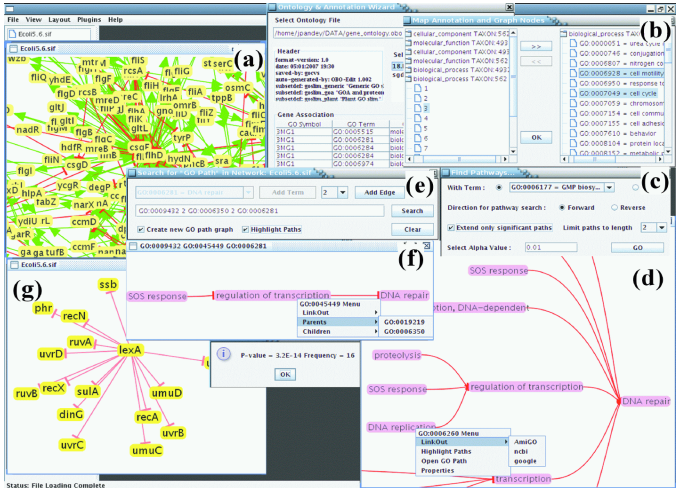


James Faeder
University of Pittsburgh
Department of Computational Biology

Collaborators
Thierry Emonet
William Hlavacek
Rick Stevens
Chris Langmead

Pathways, Cells, and Organelles

Name: Ananth Grama
Title: Professor of Computer Science
Employer/Affiliation: Purdue



Current Area of Research Interest

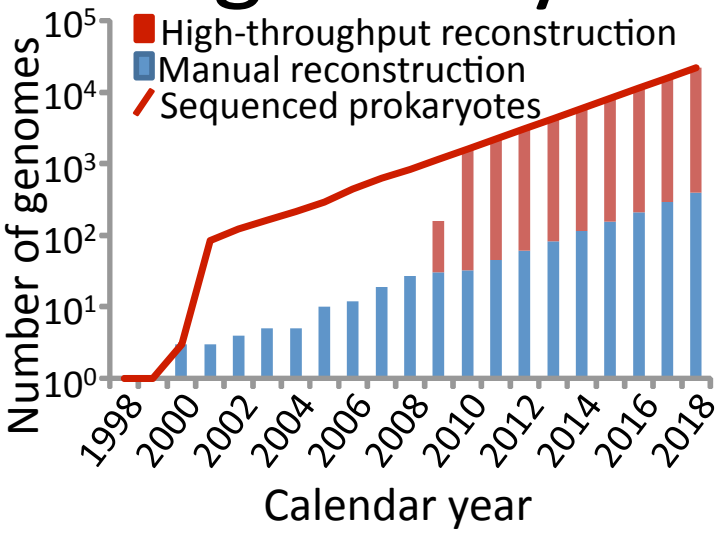
- Parallel Computing
- Computational Biology/Bioinformatics
- Computational Engineering and Sciences

Challenges that May be Addressed with Advanced Computing and Mathematics Capabilities

- High throughput network inference and modeling
- Spatiotemporal up- and down-scaling of networks
- Integration of individuals genotype (SNPs, etc.), phenotypic, and interaction data

Pathways/Metabolic and Regulatory

Christopher Henry
Assistant Scientist
Mathematics and Computer Science
Argonne National Laboratory



Current Area of Research Interest

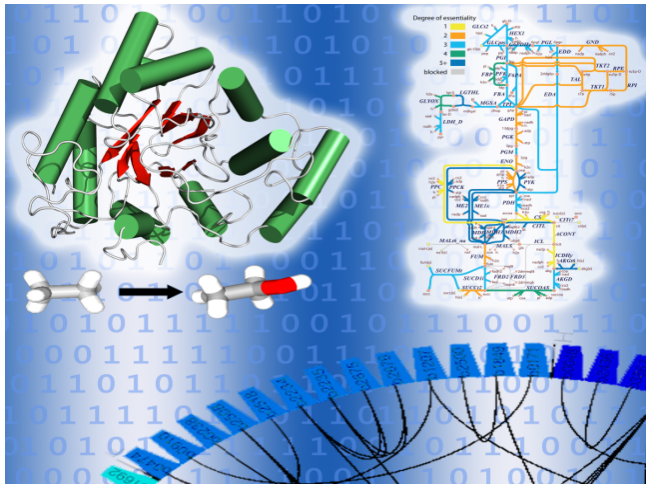
- High-throughput reconstruction, optimization and analysis of genome-scale models
- Model facilitated development of a minimal strain of *B. subtilis*
- Stochastic multi-scale modeling of cellular communities

Challenges that May be Addressed with Advanced Computing and Mathematics Capabilities

- Optimization of annotations and model stoichiometry to fit experimental data
- Optimization of regulatory network structures to fit microarray, ChIP-on-chip, and other growth phenotype data
- Scanning parameter values for dynamic models of metabolism to identify the parameter ranges that replicate observed cell behavior

Opportunities in Extreme Computing for Biology

Name: Costas D. Maranas
Title: Professor
Employer/Affiliation: PSU



Current Areas of Research Interest

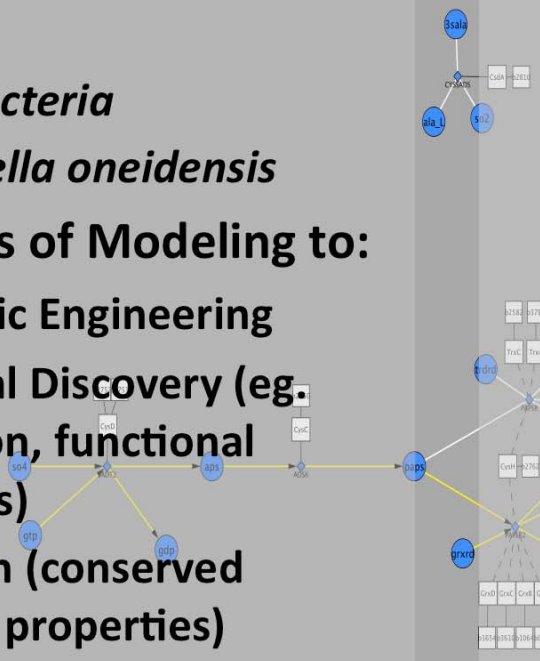
- Reconstruction, Analysis and Curation of Metabolic Networks
- Computationally guided strain design for biofuel production
- De novo protein and enzyme design

Challenges that May be Addressed with Advanced Computing and Mathematics Capabilities

- Solve larger NP-hard problems arising in metabolic network optimization
- Automatically reconstruct, test and correct genome-scale reconstructions
- Elucidate metabolic flows in genome-scale metabolic models
- Reconstruct metabolism and interdependencies of entire microbial consortia
- Enable the use of more detailed energy descriptions in protein design

Jennifer Reed
University of Wisconsin-Madison
Chemical & Biological Engineering, GLBRC

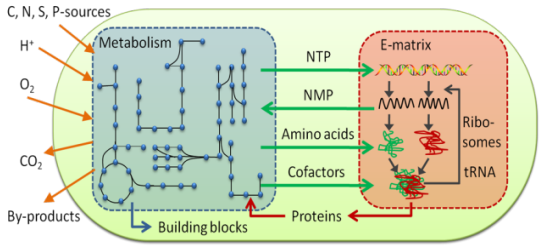
- **Research Interests**
  - Microbial metabolic & regulatory model development
    - *E. coli*
    - *Cyanobacteria*
    - *Shewanella oneidensis*
  - Applications of Modeling to:
    - Metabolic Engineering
    - Biological Discovery (eg. regulation, functional genomics)
    - Evolution (conserved network properties)
    - Microbial Interactions



- **Challenges:**
  - Mapping genome information to biological networks:
    - Transporters
    - Regulatory Networks
    - Automation
  - Large-scale models
    - Data integration
    - Large systems of non-linear equations
    - Parameter estimation
    - Isotopomer Models
  - Interactions
    - Organism-Organism
    - Organism-Natural Environment

Pathways, Cells and Organelles

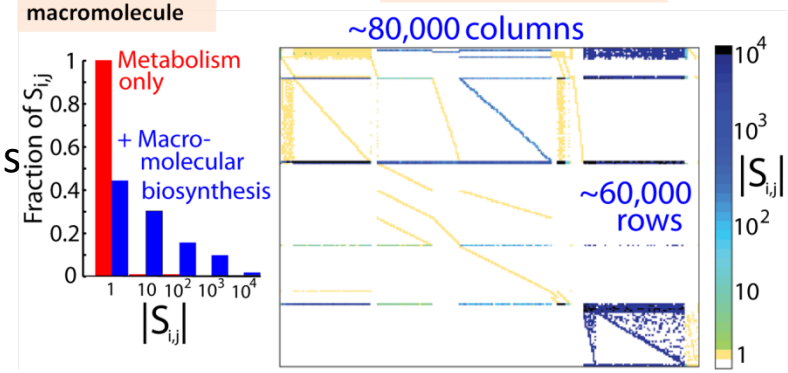
Ines Thiele
Assistant Professor
Center for Systems Biology
University of Iceland



SIZE + STIFFNESS = NUMERICAL ANALYSIS CHALLENGE

Many metabolic moieties in one macromolecule

Reaction rates over many orders of magnitude



Current Area of Research Interest

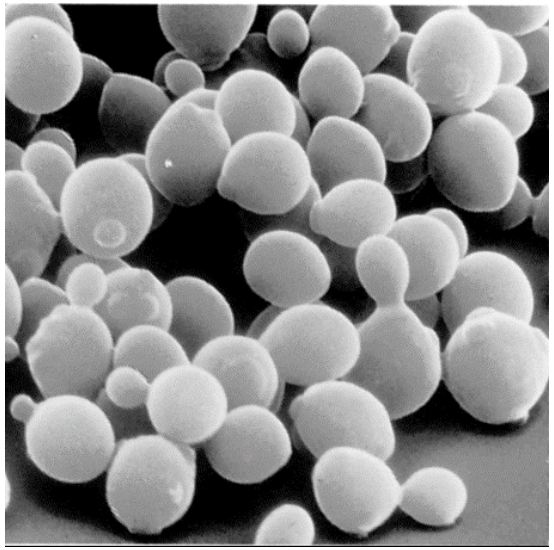
- Integrated models of multiple cellular functions
- Multi-cellular & community models
- Characterization of disease states in human metabolism

Challenges that May be Addressed with Advanced Computing and Mathematics Capabilities

- Large-scale modeling (integrated and multicellular models) will require high performing computing and algorithmic developments.
- Key reason is that the stoichiometric matrices are ill-scaled, having entries and variables distributed over many orders of magnitude.
- Advances of optimization solvers will be necessary for speed, efficiency, and accuracy of computations.

Pathways/Metabolic and Regulatory

John J. Tyson
Univ Distinguished Prof
Virginia Tech



Current Areas of Research Interest

- **Network Dynamics and Cell Physiology**
- **Deterministic and Stochastic Modeling, Hybrid Models**
- **Regulation of Cell Growth, Division and Death**
- **Differentiation of T cells and Macrophages**

Challenges that May be Addressed with Advanced Computing and Mathematics Capabilities

- **Software tools for modeling modularity of regulatory networks**
- **Parameter estimation from experimental data**
- **Bifurcation analysis of large nonlinear dynamical systems**
- **Bifurcations in stochastic dynamical systems**